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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,047	12/07/2000	Edwin F. Ullman	BEH-7385	9672

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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,047	ULLMAN ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *July 11, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 37-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 37-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *May 26, 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SDD

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 11, 2005, has been entered.

Currently, claims 1-6 and 37-46 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

Drawings were received on May 26, 2005. These drawings are accepted.

Specification

The disclosure is objected to because of the following informalities:

On p. 4, line 22, the recitation of "the target molecule" lacks antecedent basis.

On p. 4, line 23, the recitation of "the label" lacks antecedent basis.

On p. 4, line 22, the recitation of "a sandwich" is indefinite because it is not clear what members comprise said "sandwich".

On p. 4, line 25, the recitation of "the substrate" is indefinite because it is not clear whether product is physically separated from the surface or support.

On p. 4, lines 29-30, the recitation of "the free and bound receptor" lacks antecedent basis.

On p. 5, first paragraph, the relationship, if any, between "binding site" and "functional group" is indefinite.

On p. 5, lines 11-12, the mechanism by which "release of the substrate with formation of the first functional group may be accomplished by unmasking of at least some of the second functional group" is not clear.

On p. 5, lines 15-17, the mechanism by which a single substrate can "yield two functional groups that are linked together in a manner that permits binding of two specific binding reagents" is not clear.

On p. 6, lines 2-4, the mechanism underlying the recited conditional causal relationship is indefinite.

On p. 6, lines 4-5, the mechanism underlying the recited conditional causal relationship is indefinite.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-6 and 37-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The specific claim rejections under 35 USC 112, second paragraph, set forth infra, may be considered relevant to other claims not explicitly mentioned, as deemed reasonably appropriate.

In claims 1 and 44, the recitation of the term "substrate" is indefinite because Applicants' specification appears to use the term "substrate" interchangeably with "product" and "surface." For example, Applicants describe a "substrate" that is associated with, and releasable from, a "support" (see p. 4, lines 20-21, "oxidant cleavable linker may be used to attach substrate molecules... to a surface") (see p. 5, lines 11, "release of the substrate"). However, Applicants also describe a "product" that is associated with, and releasable from, a "support" and a "substrate" (see p. 4, lines 24-26, "The resulting detectable product is released from the surface or support and is physically separated from the substrate by centrifugation, decantation...") (see p. 5, lines 13-14, "the invention does not require separation of the product from the substrate").

In claim 1, the recitation of "separating the released detectable product from the substrate associated with the support" is indefinite because it is not clear whether/how said "substrate" remains associated with support after cleavage of the cleavable linker.

In claim 1, the recitation of "or indirectly" is indefinite because it is not clear what type of spatial relationship is created by "indirectly" binding or which entities are included in the binding interaction. Furthermore, a person of ordinary skill in the art cannot ascertain the standard or degree of indirectness required by "indirectly."

Claim Rejections - 35 USC § 102

Claims 1-2 and 4-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Singh et al. (US 6,770,439).

Singh et al. teach a method for amplifying a signal from a binding assay comprising the steps of providing a reaction mixture comprising: a medium suspected of containing an analyte (see col. 9, lines 16-19, "a large number of proteins in a single sample"), a first specific binding pair member bound to a support (see col. 9, lines 21-22, "One group of binding proteins is bound to a support"), a second specific binding pair member bound to a sensitizer (see col. 10, lines 22-28, "Two entities are employed... that bind to the same target moiety. One of the entities generates an active species") capable in its excited state of generating a reactive oxygen species (see col. 11, line 17, "Singlet oxygen"), wherein the proximity of the two specific binding pair members is modulated by the presence of analyte (see col. 39, lines 39-41, "The resulting complex has three components, where the target serves to link the labeled binding members to the support"), and a ~~detectable~~ substrate bound to the support through a reactive oxygen cleavable linker (see col. 10, lines 24-27, "a susceptible functionality that interacts with the active species resulting in release of the eTag reporter") (see col. 36, lines 32-35, "The solid support may have... e-tag probe covalently or non-covalently bound to the support"), incubating the reaction mixture (see col. 39, line 51, "mixture is incubated"), exciting the sensitizer causing the formation of reactive oxygen (see col. 11, line 17, "Singlet oxygen"), which cleaves the cleavable linker and releases detectable <u>product</u> ~~substrate~~ from the support (see col. 10, lines 24-27, "One of the entities generates an active species. The other entity has a susceptible functionality that interacts with the active species resulting in release of the eTag reporter"), detecting the released detectable <u>product</u> ~~substrate~~ (see Abstract, "Detection involves the release of identifying tags as a consequence of target recognition"), wherein the step of detecting comprises the steps of: separating the released detectable <u>product</u> ~~substrate~~ from the ~~detectable~~ substrate associated with the support (see col. 36, lines 19-21, "the subject heterogeneous assays require that the unbound labeled reagent be separable from the bound labeled reagent"), adding to the

separated released detectable product ~~substrate~~, a third specific binding pair member capable of binding directly to the released detectable product ~~substrate~~, allowing the third specific binding pair member to bind, and detecting the bound third specific binding pair member (see col. 40 ~~29~~, lines 25-41 ~~6-8~~, "e-tags may be reacted with detectable labels" "detectable label may be part of the reagent cleaving the cleavable bond" ~~"biotin and strept/avidin... digoxin or derivative thereof and antidigoxin~~).

With respect to claim 2, Singh et al. teaches a method for amplifying a signal from a binding assay wherein the proximity of the first and second specific binding pair members results from the binding of the first and second specific binding pair members to the analyte (see col. 39, lines 35-41, "sandwich mode", "The resulting complex has three components, where the target serves to link the labeled binding members to the support"), the sensitizer is a photosensitizer (see col. 11, lines 6-7, "squarate derivatives"), the reactive oxygen is singlet oxygen (see col. 11, lines 6-7, "singlet oxygen"), and the excitation step comprises irradiation with light (see col. 10, lines 18-19, "photoactivated excited species").

With respect to claims 4-6, Singh et al. teaches a method for amplifying a signal from a binding assay wherein the reactive oxygen cleavable linker comprises enamines (see col. 11, line 20), imidazole, oxazole, and thiazole (see col. 12, lines 29-30).

Claim Rejections - 35 USC § 103

Claims 3 and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (US 6,770,439) in view of Oh & Sternberg (US 5,851,778).

Singh et al. teach a method for amplifying a signal from a binding assay as described supra. In addition, Singh et al. teach a method wherein the analyte, first specific binding pair member, and second specific binding pair member are polynucleotides (see Figs. 3A, 3B), the substrate comprises digoxigenin and ~~digoxigenin-linked~~ biotin (see col. 29, lines 6-8, "biotin and strept/avidin... digoxin or derivative thereof and antidigoxin), and detection employs avidin and anti-digoxigenin antibodies (see col. 29, lines 6-8, "biotin and strept/avidin... digoxin or derivative thereof and antidigoxin) bound to a member of a signal producing system.

Singh et al. do not teach a detectable product ~~substrate~~ comprising digoxigenin-linked biotin.

However, Oh & Sternberg teach the use of digoxigenin-linked biotin (see col. 16, lines 30-38, "other tridentates", "digoxin") in energy transfer assays (see col. 17, lines 54+). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method for amplifying a signal from a binding assay with the use of digoxigenin-linked biotin because Oh & Sternberg discovered that tridentate conjugates do not require "expensive isolation and characterization procedures of prior art reagents" and exhibit "longer shelf life" than prior art counterparts (see col. 18, lines 51-63).

Claims 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (US 6,770,439) in view of Oh & Sternberg (US 5,851,778).

Singh et al. teach a method for amplifying a signal from a binding assay comprising the steps of providing a reaction mixture comprising: a medium suspected of containing an analyte (see col. 9, lines 16-19, "a large number of proteins in a single sample"), a first specific binding pair member bound to a support (see col. 9, lines 21-22, "One group of binding proteins is bound to a support"), a second specific binding pair member bound to a sensitizer (see col. 10, lines 22-28, "Two entities are employed... that bind to the same target moiety. One of the entities generates an active species") capable in its excited state of generating a reactive oxygen species (see col. 11, line 17, "Singlet oxygen"), wherein the proximity of the two specific binding pair members is modulated by the presence of analyte (see col. 39, lines 39-41, "The resulting complex has three components, where the target serves to link the labeled binding members to the support"), and a ~~detectable~~ substrate bound to the support through a reactive oxygen cleavable linker (see col. 10, lines 24-27, "a susceptible functionality that interacts with the active species resulting in release of the eTag reporter") (see col. 36, lines 32-35, "The solid support may have... e-tag probe covalently or non-covalently bound to the support"), incubating the reaction mixture (see col. 39, line 51, "mixture is incubated"), exciting the sensitizer causing the formation of reactive oxygen (see col. 11, line 17, "Singlet oxygen"), which cleaves the cleavable linker and releases detectable <u>product</u> ~~substrate~~ from the support (see col. 10, lines 24-27, "One of the entities generates an active species. The other entity has a susceptible functionality that interacts with the active species resulting in release of the eTag reporter"), detecting the released detectable <u>product</u> ~~substrate~~ (see Abstract, "Detection involves the release of identifying tags as a consequence of target recognition").

Singh et al. do not teach a detectable substrate comprising digoxigenin-linked biotin.

However, Oh & Sternberg teach the use of digoxigenin-linked biotin (see col. 16, lines 30-38, "other tridentates", "digoxin") in energy transfer assays (see col. 17, lines 54+). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method for amplifying a signal from a binding assay with the use of digoxigenin-linked biotin because Oh & Sternberg discovered that tridentate

conjugates do not require "expensive isolation and characterization procedures of prior art reagents" and exhibit "longer shelf life" than prior art counterparts (see col. 18, lines 51-63).

Response to Arguments

In prior Office Action, claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of the term "or indirectly". In response, Applicants appear to argue that the term "indirectly" requires "a complex of two or more sbp members which is capable of binding the other analyte or assay components" (see Applicants' reply, p. 7, third and fourth paragraphs). Applicants' argument has been carefully considered but is not persuasive because claim 1 does not appear to reference "a complex of two or more sbp members which is capable of binding the other analyte or assay components" and Examiner is reluctant to import the limitations of Applicants' argumentation into claim 1.

In prior Office Action, claims 3 and 46 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it was not clear how the "step of detecting the released detectable substrate..." was incorporated into the method of claim 1. In addition, the purpose of using both "avidin" and "anti-digoxigenin antibodies" to detect a single substrate was not clear. In addition, the recitation of "signal producing system" was considered indefinite. Applicants' amendment and/or argumentation are sufficient to overcome these rejections. Accordingly, these rejections are withdrawn.

In prior Office Action, claims 1-2 and 4-6 were rejected under 35 U.S.C. 102(e) as being anticipated by Singh et al. (US 6,770,439). In response, Applicants rejected Examiner's proposition that Singh et al. describe a "capture ligand" or "capture agent" used as a detectable label after the e-tag reporters are released or cleaved (see Applicants' reply, p. 10, first full paragraph). Examiner respectfully traverses Applicants' rejection. However, in the interest of furthering prosecution, the current Office Action is amended to further clarify and more distinctly point out the grounds for rejection set forth in prior Office

Actions. Applicants' argumentation related to this issue is now believed to have been rendered moot. Reconsideration is earnestly solicited.

In prior Office Action, claims 3 and 37-46 were rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (US 6,770,439) in view of Oh & Sternberg (US 5,851,778). In response, Applicants argue that Oh & Sternberg "has no relevance to the teachings of Singh and, thus, one skilled in the art would not be motivated to use the tridentate conjugate of Oh in the method of Singh" (see Applicants' reply, p. 11, second full paragraph). Applicants' argument has been carefully considered but is not persuasive because Oh & Sternberg provide a general teaching of a reagent for use in "analyte assays" (see Title). Insofar as Applicants' invention, as currently claimed, is also a general disclosure of an "analyte assay", the teachings of Oh & Sternberg appear highly relevant.

Conclusion

No claims are allowed at this time.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

> Hearst et al. (US 5,184,020) is cited for their teaching of methods involving a "substrate" comprising biotin connected to a reporter moiety via a cleavable linker (see e.g., col. 17, lines 45-62), which is relevant to claims 3 and 44.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv

LONG V. LE
SUPERVISORY PATENT EXAMINER
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09/19/01